UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/815,119	03/31/2004	Tian Wen	20335-00186	6566

28534 7590 08/06/2008

MIRICK, O'CONNELL, DEMALLIE & LOUGEE, LLP
1700 WEST PARK DRIVE
WESTBOROUGH, MA 01581

EXAMINER	
FUBARA, BLESSING M	
ART UNIT	PAPER NUMBER
1618	
MAIL DATE	DELIVERY MODE
08/06/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/815,119	WEN ET AL.	
	Examiner	Art Unit	
	BLESSING M. FUBARA	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 April 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-25,27 and 28* is/are pending in the application.

4a) Of the above claim(s) *24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22, 23 and 25, 27 and 28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *04/03/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The examiner acknowledges receipt of IDS, amendment and remarks filed 04/03/08. Claim 26 is canceled. Claim 22 is amended. Claims 22-25, 27 and 28 are pending.

Response to Arguments

Rejections that are not reiterated herein are withdrawn.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 22, 23, 25, 27 and 28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is new matter.

Amended claim 22 requires the application of the semisolid compositions to produce increased blood flow through the region within thirty minutes. This particular effect due to the administration of the composition does not appear to have support from the specification as originally filed. Applicant pointed to cancelled claim 26 and paragraphs [0009], [0014] and [0079] of the published application as providing support for the amendment. However, the examiner is unable to find the support in the specification. Applicant may point to the specification for the support or delete the new matter from the claims to overcome the rejection.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 22, 23, 25 and 28 remain rejected under 35 U.S.C. 102(b) as being anticipated by Buyuktimkin et al. (US 6,046,244) for reasons of record and reiterated herein and modified to reflect the amendment.

Buyuktimkin provides a semi solid composition comprising prostaglandin E_1 for sustained delivery of the prostaglandin E_1 that addresses transdermal/topical delivery of prostaglandin E_1, which Buyuktimkin recognizes is a "vasodilator useful to maintain open blood vessels and therefore, to treat peripheral vascular disease among other ailments. While the potential benefits from transdermal delivery of prostaglandin" E_1 "have long been recognized, prior efforts at developing a topical composition for prostaglandin delivery have not been fully successful," (column 1, lines 27-34) with the prostaglandin" E_1 meeting claim 25. The composition of Buyuktimkin comprises prostaglandin E_1, polysaccharide gum, lipophilic compound, penetration enhancer and buffer system that is capable of buffering the composition at a pH of about 3 to about 7.4 (abstract; column 2, lines 9-28) meeting claim 22. The composition is applied to the skin of a patient (column 8, lines 1-19) meeting the method of claim 22 and the tissue requirement of claim 23 since the purpose of Buyuktimkin is to transdermally administer prostaglandin containing composition to treat peripheral vascular disease to maintain open blood vessels. Specific polysaccharide present in the composition of

Buyuktimkin is galactomannan (column 2, line 49; column 5, lines 37-58) meeting the polymer thickener of claim 22. The penetration enhancer is substituted alkanoate such as dodecyl 2-(N,N dimethylamino)-propionate (DDAIP) (column3, lines 5-54) meeting the limitation of previous claim 26 that is now incorporated into claim 22 and also meets claim 27. The lipophilic component is aliphatic C_1-C_8 alcohol or aliphatic C_8-C_{30} ester (abstract; column 2, lines 15-17; column 6, lines 28-31) meeting claims 22 and 28. The recitation in the amended claim of "where application of the semisolid composition produces an increase in blood flow through the region of vasospasm within thirty minutes of the application" is effect of the composition and the application of the composition of Buyuktimkin would inherently produce the effect within the time recited. Buyuktimkin meets the limitations of the claims.

Response to Arguments

5. Applicant's arguments filed 04/03/08 have been fully considered but they are not persuasive.

6. Applicant acknowledges that Buyuktimkin teaches similar composition used in the claims but argues that Buyuktimkin does not anticipate the claims because Buyuktimkin does not topically apply that composition to a region of a subject's tissue requiring treatment of vasospasm in an effective amount and because vasospasm is not peripheral vascular disease. To this end, applicant has provided several references including what vasospasm is, that is, "vasospasm" is a "sudden decrease in the internal diameter of blood vessel that results from contraction of smooth muscle within the wall of the vessel" that "causes decrease in blood flow, but increase in systemic vascular resistance."

Thus, the examiner disagrees. Since the goal of Buyuktimkin is to keep open blood vessels, the topical administration of similar or same composition by Buyuktimkin would inherently treat vasospasm. The definition of vasospasm provided by the applicant supports the examiners position. The definition is, "the sudden decrease in the internal diameter of a blood vessel that results from contraction of smooth muscle within the wall of the vessel. This causes a decrease in blood flow, but and increase in systemic vascular resistance."

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 22, 23, 25, 27 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Buyuktimkin et al. (US 6,046,244) in view of Clifford et al., ("Treatment of vasospastic

disease with prostaglandin E1," in Br Med J. 1980 October 18; 281(6247): 1031–1034) reasons of record and reiterated herein.

Buyuktimkin is described above as disclosing a composition comprising prostaglandin E_1, penetration enhancer, polymer thickener, lipophilic component and buffer system that maintains the composition at a pH of about 3 to about 7.4 for the purpose of transdermal/topical administration for treating conditions that are treatable with prostaglandin E_1 such as maintaining open blood vessels (column 1, lines 27-33) and male impotency and other ailments (column 8, lines 6-8). Although, Buyuktimkin does not use the term vasospasm, keeping open blood vessels is treating narrowing of the blood vessels. However, Clifford discloses that prostaglandin E_1 is a vasodilator and potent inhibitor of platelet aggregation and is used to treat vasospastic disease. Therefore, transdermal application of a composition comprising a known vasodilator, prostaglandin E_1, would maintain open blood vessels as taught by Buyuktimkin and therefore treat vasospasm when applied to the skin of a patient (column 8, line 12 of Buyuktimkin) as evidenced by the positive teaching of treating vasospastic disease with prostaglandin E_1. Therefore, taken the teaching of Buyuktimkin in view of the evidence provided by Clifford, the ordinary skilled artisan would reasonably expect to successfully treat vasospasm or maintain open blood vessels by transdermally/topically applying the semi solid composition of Buyuktimkin to the skin of a patient.

Response to Arguments

10. Applicant's arguments filed 04/03/08 have been fully considered but they are not persuasive.

11. Applicant argues that Clifford "would not render obvious the present claims" because Clifford relates to intravenous infusion of prostaglandin E1 to treat severe vasospastic disease (Raynaud's); that Clifford recognizes that management of patients who suffer from sever Raynaud's phenomenon with or without trophic skin changes remains controversial, and that "vasodilators, …are used with varying effect." Applicant further states that the present invention topically applies semisolid composition for delivery of prostaglandin E1 and that prostaglandin delivery has been shown to be difficult and inconsistent, and one would not expect that a topical delivery of prostaglandin E1 using the semi solid composition Buyuktimkin would be successful for delivery of prostaglandin to the endothelium of the vasculature since the endothelium of the vasculature is the pharmacological site of activity; therefore, applicant concludes that one skilled in the art would not expect that topical delivery of a semi solid composition of Buyuktimkin would successfully deliver prostaglandin to the endothelium of the vasculature for effective treatment of vasospasm. Applicant further argues that Clifford recognizes the difference between peripheral vascular disease and vasospasm and while recognizing that prostaglandin infusion was found to be effective for treating vasospasm, notes that further studies are warranted to determine whether prostaglandin has a role in treating peripheral vascular disease.

12. The examiner disagrees. The teachings of Buyuktimkin taken in view of Clifford renders obvious the claims because i) Clifford is relied upon for teaching that the prostaglandin E1 is a vasodilator and potent inhibitor of platelet aggregation and is used top treat vasospasm and the fact that Clifford teaches that prostaglandin treats vasospasm is admitted by applicant on the record in the remarks. ii) Clifford is not relied upon for administering prostaglandin by

infusion. iii) Applicant's argument is centered on Clifford and by centering the argument on Clifford, applicant is arguing against Clifford as an individual reference. In the present case a combination of teachings is used in the rejection under this section; and one cannot show non-obviousness by attacking the references individually when combination of references is used. iv) In regards to topical administration of prostaglandin, which applicant says shows inconsistent efficacy and difficult to administer therapeutically effective dose, it is noted that Buyuktimkin successfully applies prostaglandin topically to open blood vessels. It is further noted that since Buyuktimkin uses prostaglandin to open blood vessels and Clifford teaches that prostaglandin is used to treat vasospasm, the prior art has shown therapeutic utility and applicant's opinion lack of efficacy of the prostaglandin in the Clifford or the Buyuktimkin references, individually or in combination does not overcome the rejections under 35 USC 103 because efficacy is not a requirement for the ordinary skilled artisan to carry out the teachings of the prior art. ("[P]roof of efficacy is not required for a prior art reference to be enabling for purposes of anticipation," see Impax Labs. Inc. v. Aventis Pharm. Inc., 468 F.3d 1366, 1383, 8 USPQ2d 1001, 1013 (Fed. Cir. 2006)).

13. No claim is allowed.

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BLESSING M. FUBARA whose telephone number is (571)272-0594. The examiner can normally be reached on 7 a.m. to 5:30 p.m. (Monday to Thursday).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

/Blessing M. Fubara/
Examiner, Art Unit 1618